Embryonic Stem Cell-Derived Hematopoietic Stem Cells: Challenges in Development, Differentiation, and Immunogenicity.

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Public Summary:
Embryonic stem cells (ESC) can potentially be manipulated in vitro to differentiate into cells and tissues of all three germ layers. This pluripotent feature is being exploited to use ESC-derived tissues as therapies for degenerative diseases and replacement of damaged organs. Although their potential is great, the promise of ESC-derived therapies will be unfulfilled unless several challenges are overcome. In this review, we discuss the challenges to in vitro development of a bona fide ESC-derived hematopoietic stem cell and their differentiation fate in vivo, and provide suggestions to predict the immunogenicity of specific ESC-derived hematopoietic populations before transplantation that could be used to prevent their rejection after transplantation into an adult host.

Scientific Abstract:
Embryonic stem cells (ESC) can potentially be manipulated in vitro to differentiate into cells and tissues of all three germ layers. This pluripotent feature is being exploited to use ESC-derived tissues as therapies for degenerative diseases and replacement of damaged organs. Although their potential is great, the promise of ESC-derived therapies will be unfulfilled unless several challenges are overcome. For example, inefficient production of ESC-derived tissues before transplantation, inability of ESC-derived tissues to integrate well into the adult microenvironments due to developmental stage incompatibility, or active immune rejection of the ESC-derived graft are all potential challenges to successful ESC-derived therapies. One way to induce immunological tolerance to allogeneic tissues is via the establishment of mixed hematopoietic chimerism in which the host and donor cells are educated to recognize each other as "self". Proof of principle that in vitro cultured ESC-derived hematopoietic progenitors can be transplanted and induce immunological tolerance to allogeneic tissues exists in mouse models. In this review, we discuss the challenges to in vitro development of a bona fide ESC-derived hematopoietic stem cell and their differentiation fate in vivo, and provide suggestions to predict the immunogenicity of specific ESC-derived hematopoietic populations before transplantation that could be used to prevent their rejection after transplantation into an adult host.